产品名称：**AZD5582**
产品别名：**AZD5582**

生物活性：		
Description	AZD5582 is an antagonist of the inhibitor of apoptosis proteins (IAPs), which binds to the BIR3 domains cIAP1, cIAP2, and XIAP with IC50s of 15, 21, and 15 nM, respectively[1].	
In Vitro	AZD5582 (20 nM; 48 hours) inhibited cell viability by cooperation with IFNγ or viral double-stranded RNA (dsRNA) in H1975 NSCLC cells[2]. AZD5582 (20 nM; 17 or 25 hours) down-regulates cIAP-1, activates RIPK1(upstream regulator of caspase-8), and triggers the activation of extrinsic (caspase-8) and intrinsic (caspase-9) apoptosis pathways, causing the cleavage of caspase-3 and caspase-7[2]. AZD5582 (20 nM; 48 hours) involves in apoptosis due to induction of cell death and active caspase-3/ -8 activities by AZD5582 and IFNγ co-treatment in HCC827 NSCLC cells[2].	
	Cell Viability Assay[2]	
	Cell Line:	H1975 NSCLC cell line
	Concentration:	20 nM
	Incubation Time:	48 hours
	Result:	Cooperated with IFNγ or viral double-stranded RNA (dsRNA) to inhibit cell viability even cell death.
	Western Blot Analysis[2]	
	Cell Line:	H1975 NSCLC cell line
	Concentration:	20 nM
	Incubation Time:	17 or 25 hours
	Result:	Down-regulated cIAP-1, activated RIPK1 (upstream regulator of caspase-8), triggered the cleavage (activation) of caspase-3,7,8 and 9.
	Apoptosis Analysis[2]	
	Cell Line:	HCC827 NSCLC cell line
	Concentration:	20 nM
	Incubation Time:	48 hours
	Result:	Had a inhibitory effect on cell viability by cooperating with IFNγ.
In Vivo	AZD5582 (intravenous injection; 0.1-3.0 mg/kg; once a week; 2 weeks) causes degradation of cIAP1 and caspase 3 cleavage in tumor cells, and after a two-week treatment, the tumors largely resolved; when the mice are given a medium dose (0.5 mg/kg) of AZD5582, cIAP1 degrades after administration, but it takes a while time to reach apoptosis-inducing effect[1].	
	Animal Model:	MDA-MB-231 xenograft-bearing mice
	Dosage:	0.1mg/kg,0.5mg/kg,3.0mg/kg
	Administration:	Intravenous injection; once a week; 2 weeks
	Result:	Resulted in cIAP1 degradation and caspase-3 cleavage within tumor cells and causes substantial tumor regressions following two weekly doses of 3.0 mg/kg

In Vitro:

DMSO : ≥ 66.25 mg/mL (65.25 mM)

* "≥" means soluble, but saturation unknown.

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg

<table>
<tr><td rowspan="5">Solvent&Solubility</td><td rowspan="4">Preparing Stock Solutions</td><td></td><td></td><td></td><td></td></tr>
<tr><td>1 mM</td><td>0.9849 mL</td><td>4.9247 mL</td><td>9.8494 mL</td></tr>
<tr><td>5 mM</td><td>0.1970 mL</td><td>0.9849 mL</td><td>1.9699 mL</td></tr>
<tr><td>10 mM</td><td>0.0985 mL</td><td>0.4925 mL</td><td>0.9849 mL</td></tr>
<tr><td colspan="5">*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。
储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。
In Vivo:
请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：
——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶
1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline
Solubility: ≥ 2.5 mg/mL (2.46 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (2.46 mM，饱和度未知) 的澄清溶液。
以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 10% DMSO →90% corn oil
Solubility: ≥ 2.5 mg/mL (2.46 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (2.46 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。
以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</td></tr>
<tr><td>References</td><td colspan="5">[1]. Hennessy EJ, et al. Discovery of a novel class of dimeric Smac mimetics as potent IAP antagonists resulting in a clinical candidate for the treatment of cancer (AZD5582). J Med Chem. 2013 Dec 27;56(24):9897-919.
[2]. Qin Hao et al,Interferon-γ and Smac mimetics synergize to induce apoptosis of lung cancer cells in a TNFα-independent manner,Cancer Cell Int. 2018; 18: 84.</td></tr>
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